which in turn depends indirectly from claim 6. Claims 9 and 6 recite elected sequences. It is submitted that this dependency underscores the impropriety of the requirement for election of a sequence. A similar situation exists with respect to claims 17-25. Accordingly, the Examiner is again urged to reconsider the requirement for sequence election. (For the Examiner's information, a Petition From Restriction For Requirement is being filed concurrently herewith.)

The specification has been amended to correct the spelling errors noted by the Examiner, to make reference to the PCT application from which this case derives, to include the heading "Brief Description of the Drawings", to include sequence identifiers at pages 19, 20 and 47 (as regards page 52, the Examiner is requested to note page 27 of the June 26, 2001 Amendment which introduces appropriate identifiers) and to revise the drawing descriptions. An Abstract of the Disclosure has also been added. Nothing further is believed to be required (various of the headings to which the Examiner refers are merely suggested, not required).

The claims have been revised to define the invention with additional clarity. Basis for the hybridization conditions recited in claims 6 and 14 is found on page 24,

lines 7 to 9 of the specification. Basis for influencing the growth of a plant as recited in claim 46 is found on page 30, line 1 of the specification. Claims 2, 7-9, 30, 31, 55 and 56 have been cancelled. That the claims have been revised/cancelled should not be taken as an indication that Applicants agree with any view expressed by the Examiner. Rather, the revisions are made merely to advance prosecution and Applicants reserve the right to pursue any deleted subject matter in a continuation application.

Claims 1-3, 6-9 and 14-16 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Withdrawal of the rejection is submitted to be in order in view of the above-noted claim revisions. Reconsideration is requested.

Claims 1-2, 6-9, 14-16, 30-31 and 55-56 stand rejected under 35 USC 112, first paragraph, as allegedly being non-enabled. Claims 2, 7-9, 16, 30, 31, 55 and 56 have been cancelled, rendering moot rejections thereof. Withdrawal of the rejection of the remaining claims is in order for the reasons that follow.

Claim 1 is specifically directed at a polynucleotide encoding the Rht polypeptide obtained from wheat which comprises SEQ ID NO:104.

The present application provides both guidance and exemplification of the isolation of the wild-type wheat Rht sequence (page 46, line 4 to page 47, line 24) and also the Rht-D1c dominant mutant allele (page 48, line 22 to page 50, line 7). Methods of screening libraries and manipulating DNA are well known in the art and are discussed at length in the specification, for example, from page 21 line 23 to page 25 line 14. A person skilled in the art is taught what to screen and with what to screen. Given this information and knowledge of routine experimental methods, the skilled person is fully able to practice the invention across the full scope of claim 1. This is acknowledged by the Examiner on page 9 of the Action, where the specification is described as 'being enabling for an isolated polynucleotide encoding Rht polypeptide from wheat comprising SEQ ID NO:104 or 7'. Claim 1 as amended, therefore, meets the requirements of 35 USC § 112, first paragraph.

Claims 6 and 14 recite a polynucleotide that hybridizes to the wheat Rht coding sequence under particular stringency conditions and that encodes a polypeptide that has a specific activity. Claim 6 further recites a partial amino acid sequence. Claim 15 is dependent on claim 14 and further specifies that the

polypeptide is wheat Rht with a particular defined deletion.

The specification provides complete guidance to a skilled person regarding the obtention of polynucleotides within the scope of these claims. For example, pages 45, line 13 to page 47, line 24 exemplify the screening of a database to identify an EST to the corresponding gene in rice and the further screening of libraries from wheat and maize to identify the maize D8 and wheat Rht genes. Hybridization is further discussed from page 21, line 23 to page 25, line 14 and suitable probes are discussed on page 15, line 5 to page 16, line 27. To isolate further polynucleotides within the scope of these claims, a person of skill in the art simply needs to screen a DNA library with the probes described (or other probes which can be easily designed by such a person from the disclosed sequences). As described above, methods for screening libraries are routine in the art and are exemplified in the present application for wheat Rht, maize D8 and alleles thereof. Alternative approaches involving database analysis and subsequent sequencing are exemplified by the rice homologue sequence shown in figures 6a and 6b.

The cloning of the maize and wheat genes by Applicants provides working examples of the successful practice of

these screening methods. A person skilled in the art is familiar with methods of screening and DNA manipulation and full guidance as to the application of these methods to the present subject-matter is found in the specification, including worked examples. There is therefore no undue experimentation required for a skilled person to identify polynucleotides which fall within the scope of claims 6, 14 and 15 and these claims meet the requirements of 35 USC §112, first paragraph. Reconsideration is thus requested.

Claims 1-2, 6-9, 14-16, 28-46 and 55-56 stand rejected under 35 USC 112, first paragraph, as allegedly lacking written description. Claims 2, 7-9, 16, 30, 31, 55 and 56 have been cancelled, rendering moot the rejection of these claims. Withdrawal of the rejection as it relates to the remaining claims is in order for the reasons that follow.

As described above, claim 1 is directed specifically to the polynucleotide that encodes the Rht polypeptide obtained from wheat. Not only is the source of the polypeptide defined but the polypeptide is further characterized by the presence of the GA transduction element (SEQ ID NO:104) and the specified Rht activity.

The specification exemplifies the wild-type wheat Rht polypeptide sequence (SEQ ID NO: 7) and a polynucleotide which encodes this polypeptide (SEQ ID NO:14). The

specification contemplates variant sequences and teaches how Rht protein variants and alleles can be cloned and sequenced using DNA manipulation methodology which is routine in the art. This is exemplified using PCR (see page 49) and the partial (variant) sequence of the Rht-D1c mutant is provided in figure 12.

The specification teaches that the Rht polypeptide is responsible for GA antagonized growth inhibition. Assays for such inhibition (which indicates an active Rht polypeptide) are well known in the art and are discussed on page 5, lines 25 to page 7, line 2. Thus a person of skill in the art is readily able to determine if a protein has GA antagonized growth inhibition activity as set out in claim 1.

The Examiner has indicated that all the claims presently under consideration (including claim 1) are free of the prior art i.e. are novel and non-obvious. There is a single species disclosed (SEQ ID NO: 14) that is within the scope of the claimed genus. There is actual reduction to practice of the disclosed species (SEQ ID NO: 14). The genus of polynucleotides which fall within the scope of claim 1 do not have substantial variation, since they all encode a polypeptide obtained from wheat which comprises the partial sequence SEQ ID NO: 104 and possesses the GA

antagonized growth inhibition activity. The single species is representative of the genus because all members of the genus encode the wheat Rht protein which includes a distinctive GA transduction sequence (SEQ ID NO:14) and Applicants teach numerous assays that are known in the art that can be used to identify Rht proteins which have GA antagonized growth inhibition activity.

One of skill in the art would conclude that Applicants were in possession of the necessary common attributes possessed by members of the genus defined by claim 1. Claim 1 therefore meets the requirements of 35 USC §112, first paragraph.

As described above, claim 6 recites a polynucleotide which hybridizes to the wheat Rht coding sequence under the stated stringent conditions and which encodes a polypeptide which has GA antagonized growth inhibition activity and which comprises a particular amino acid sequence.

The specification exemplifies the screening of wheat and maize libraries with a rice EST sequence using hybridization techniques and the subsequent cloning of the maize D8 and wheat Rht sequences. The cloning of mutant alleles of D8 and Rht is also exemplified.

Hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the

art at the time of filing, as evidenced by Sambrook et al Molecular Cloning: a Laboratory Manual (1989) Cold Spring Harbor Press NY, which is incorporated into the specification by reference (page 11 lines 23-25).

The Examiner has indicated that all the claims presently under consideration are free of the prior art i.e. are novel and non-obvious. There is a single species disclosed (SEQ ID NO: 14) that is within the scope of the claimed genus. Thus, there is actual reduction to practice of the disclosed species.

A person of skill in the art would not expect substantial variation among species encompassed within the scope of these claims because the highly stringent hybridization conditions set forth in claim 6 yield structurally similar DNAs. Furthermore, the DNAs are required to encode a polypeptide comprising (SEQ ID NO:104) which has a specific activity (GA antagonized growth inhibition). Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to establish that Applicants were in possession of the claimed invention.

One of skill in the art would conclude that Applicants were in possession of the necessary common attributes possessed by members of the genus defined by claim 6 and this claim therefore meets the requirements of 35 USC §112, first paragraph.

As described above, claim 14 recites a polynucleotide which hybridizes to the wheat Rht coding sequence under the stated stringent conditions and which encodes a polypeptide which confers GA insensitive dwarfism on a plant

The specification exemplifies the screening of wheat (variety 'Chinese spring') and maize (line 'B73N') libraries by hybridization with a rice EST and the subsequent cloning of the maize D8 and wheat Rht sequences. Examples of the cloning and sequencing of mutant alleles (D8-1, D8-2023, and Rht-D1c) responsible for known dwarf phenotypes (see page 3 lines 6 to 25) are also provided in the specification on page 48, line 22 to page 50, line 7.

Hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the art at the time of filing, as evidenced by Sambrook et al Molecular Cloning: a Laboratory Manual (1989) Cold Spring Harbor Press NY, which is incorporated into the specification by reference (page 11 lines 23-25). A person skilled in the art would have no difficulty in screening a

library from a plant with a known mutant Rht phenotype as described in the specification to isolate a polynucleotide within the scope of claim 14.

The Examiner has indicated that all the claims presently under consideration (including claims 14 and 15) are free of the prior art i.e. are novel and non-obvious. There is a single species disclosed (SEQ ID NO: 12) that is within the scope of the claimed genus. Thus, there is actual reduction to practice of the disclosed species.

A person of skill in the art would not expect substantial variation among species encompassed within the scope of these claims because the highly stringent hybridization conditions set forth in claim 14 yield structurally similar DNAs . Furthermore, the DNAs are required to encode a polypeptide which confers GA insensitive dwarfism. This is a readily determined phenotypic trait as described on page 3 line 6 to page 4 line 17 of the specification.

Thus, the single species disclosed is representative of the genus defined in claim 14, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that Applicants were in possession of the claimed invention.

One of skill in the art would conclude that Applicants were in possession of the necessary common attributes possessed by members of the genus defined by claim 14 and this claim therefore meets the requirements of 35 USC §112, first paragraph.

Claim 15 is dependent on claim 14 and defines a more specific genus in which the encoded polypeptide is the wheat Rht polypeptide with the sequence of SEQ ID NO:104 deleted.

Given the comments above in relation to the previous claims, it is clear that one of skill in the art would conclude that Applicants were in possession of the necessary common attributes possessed by members of the genus defined by claim 15 and this claim therefore meets the requirements of 35 USC §112, first paragraph.

Reconsideration is requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned "**Version With Markings To Show Changes Made**."

HARBERD et al -- Serial No.: 09/485,529

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning at page 19, line 6:

As is well-understood, homology at the amino acid level is generally in terms of amino acid similarity or identity. Similarity allows for "conservative variation", i.e. substitution of one hydrophobic residue such as isoleucine, valine, leucine or methionine for another, or the substitution of one polar residue for another, such as arginine for lysine, glutamic for aspartic acid, or glutamine for asparagine. Similarity may be as defined and determined by the TBLASTN program, of Altschul et al. (1990) J. Mol. Biol. 215: 403-10, which is in standard use in the art, or more preferably GAP (Program Manual for the Wisconsin Package, Version 8, September 1994, Genetics Computer Group, 575 Science Drive, Madison, USA), which uses the algorithm of Needleman and Wunsch to align sequences. Suitable parameters for GAP include the default parameters, a gap creation penalty = 12 and gap extension penalty = 4, or gap creation penalty 3.00 and gap extension penalty 0.1. Homology may be over the full-length of the Rht sequence of Figure 3b, or may more preferably be over a

contiguous sequence of 10 amino acids compared with DVAQKLEQLE (SEQ ID NO:4), and/or a contiguous sequence of 17 amino acids, compared with the 17 amino acids underlined in Figure 3b, and/or a contiguous sequence of 27 amino acids compared with DELLAALGYKVRASDMADVAQKLEQLE (SEQ ID NO:56), or [,or] a longer sequence, e.g. about 30, 40, 50 or more amino acids, compared with the amino acid sequence of Figure 3b and preferably including the underlined 17 amino acids and/or DVAQKLEQLE (SEQ ID NO:4).

The paragraph beginning at page 20, line 6:

At the nucleic acid level, homology may be over the full-length or more preferably by comparison with the 30 nucleotide coding sequence within the sequence of Figure 3a and encoding the sequence DVAQKLEQLE (SEQ ID NO:4) and/or the 51 nucleotide coding sequence within the sequence of Figure 3a and encoding the 17 amino acid sequence underlined in Figure 3b, or a longer sequence, e.g. about 60, 70, 80, 90, 100, 120, 150 or more nucleotides and preferably including the 51 nucleotide of Figure 3 which encodes the underlined 17 amino acid sequence of Figure 3b.

The paragraph beginning at page 25, line 8:

If need be, [stringencycan] stringency can be increased by increasing the temperature of the washes, and/or reducing or even omitting altogether, the SSC [ini] in the wash solution.

The paragraph beginning at page 25, line 16:

Homologues to rht mutants are also provided by the present invention. These may be mutants where the wild-type includes the 17 amino acids underlined in Figure 3b, or a contiguous sequence of 17 amino acids with at least about 10 (more preferably 11, 12, 13, 14, 15, 16 or 17) which have similarity or identity with the corresponding residue in the 17 amino acid sequence underlined in Figure 3, but the mutant does not. Similarly, such mutants may be where the wild-type includes DVAQKLEQLE or a contiguous sequence of 10 amino [aicds] acids with at least about 5 (more preferably 6, 7, 8 or 9) which have similarity or identity with the corresponding residue in the sequence DVAQKLEQLE, but the mutant does not. Nucleic acid encoding such mutant polypeptides may on expression in a plant confer a phenotype which is insensitive or unresponsive to treatment of the plant with GA, that is a mutant phenotype which is not overcome or there is no reversion to wild-type phenotype on treatment of the plant with GA (though there

may be some response in the plant on provision or depletion of GA).

The paragraph beginning at page 42, line 1:

[Figure 2:] Figures 2a-2c. DNA sequences from C15-1, 14a1 and 5a1[.]:

The paragraph beginning at page 42, line 12:

[Figure 3:] Figures 3a and 3b. Rht sequences[.]:

The paragraph beginning at page 42, line 23:

[Figure 4:] Figures 4a and 4b. D39460 sequence[.]:

The paragraph beginning at page 43, line 10:

[Figure 6:] Figures 6a and 6b. Rice EST sequence:

The paragraph beginning at page 43, line 18:

[Figure 7:] Figures 7a and 7b. Wheat C15-1 cDNA:

The paragraph beginning at page 43, line 26:

[Figure 8:] Figures 8a and 8b. Wheat 5a1 genomic clone:

The paragraph beginning at page 44, line 6:

[Figure 9:] Figures 9a and 9b. Maize 1a1 genomic clone:

The paragraph beginning at page 44, line 19:

[Figure 11:] Figures 11a-11d. Sequences of maize D8 alleles:

The paragraph beginning at page 45, line 4:

[Figure 12:] Figures 12a and 12b. Wheat rht-10 allele:

The paragraph beginning at page 47, line 3:

Figure 2a gives the complete (single-pass) DNA sequence of cDNA C15-1. We have also obtained DNA sequence for C15-10; it is identical with that of C15-1, and is therefore not shown. Figures 2b and 2c show original data from individual sequencing runs from clones 14a1 and 5a1. The sequences shown in Figure 2 can be overlapped to make a composite DNA sequence, shown in Figure 3a. This sequence displays strong homology with that of Arabidopsis GAI, as revealed by a comparison of the amino acid sequence of a predicted translational product of the wheat sequence (Rht) with that of GAI (GAI), shown in Figure 3b. In particular, the predicted amino acid sequence of the presumptive Rht

reveals a region of near-identity with GAI over the region that is missing in gai (Figure 4). Figure 4 reveals that the homology that extends beyond the gai deletion region in the rice EST is also conserved in Rht (DVAQKLEQLE (SEQ ID NO:4)), thus indicating that this region, in addition to that found in the gai deletion, is involved in GA signal-transduction. This region is not found in SCR, another protein that is related in sequence to GAI but which is not involved in GA signalling. The primers used in the above sequencing experiments are shown in Table 1.

IN THE CLAIMS:

1. (Twice Amended) An isolated polynucleotide encoding a polypeptide which comprises the amino acid sequence of a *Rht* polypeptide obtained from *Triticum aestivum*, said sequence comprising the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104),

and which on expression in a *Triticum [Aestivum] aestivum* plant provides inhibition of growth of the plant, which inhibition is antagonised by gibberellin.

3. (Twice Amended) An isolated polynucleotide according to [claim 2] claim 1 which includes the nucleotide sequence of nucleic acid [obtainable] obtained

from *Triticum [Aestivum] aestivum* encoding the *Rht* polypeptide, the nucleotide sequence including GACGAGCTGCTGGCGGCGCTCGGGTACAAGGTGCGCGCCTCCGACATGGCG (SEQ ID NO:105).

6. (Twice Amended) An isolated polynucleotide encoding a polypeptide which comprises the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104) and which on expression in a plant provides inhibition of growth of the plant, which inhibition is antagonised by gibberellin,

[wherein the polypeptide has an amino acid sequence which shows at least 80% similarity with the amino acid sequence of the *Rht* polypeptide of *Triticum Aestivum* encoded by nucleic acid obtainable from *Triticum Aestivum* which includes the nucleotide sequence GACGAGCTGCTGGCGGCGCTCGGGTACAAGGTGCGCGCCTCCGACATGGCG (SEQ ID NO:105).]

wherein said polynucleotide specifically hybridizes to the sequence of Figure 8A (SEQ ID NO: 14) at 42°C in 0.25M Na_2HPO_4, pH 7.2, 6.5% SDS, 10% dextran sulfate and a final wash at 55°C in 0.1X SSC, 0.1% SDS.

14. (Twice Amended) An isolated polynucleotide encoding a polypeptide which on expression in a plant

confers a phenotype on the plant which is gibberellin-unresponsive dwarfism or which on expression in a *rht* null mutant phenotype plant complements the *rht* null mutant phenotype, such *rht* null mutant phenotype being resistance to the dwarfing effect of paclobutrazol,

[wherein the polypeptide has an amino acid sequence which shows at least 80% similarity with the amino acid sequence of the *Rht* polypeptide of *Triticum Aestivum* encoded by nucleic acid obtainable from *Triticum Aestivum* which includes the nucleotide sequence GACGAGCTGCTGGCGGCGCTCGGGTACAAGGTGCGCGCCTCCGACATGGCG.]

wherein said polynucleotide specifically hybridizes to the polynucleotide sequence of Figure 8A (SEQ ID NO: 14) at 42°C in 0.25M Na_2HPO_4, pH 7.2, 6.5% SDS, 10% dextran sulfate with a final wash at 55°C in 0.1X SSC, 0.1% SDS.

15. (Amended) An isolated polynucleotide according to claim 14 wherein the polypeptide includes the amino acid sequence of a *Rht* polypeptide [obtainable] obtained from *Triticum [Aestivum] aestivum*, with the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104) deleted.

32. (Twice Amended) A nucleic acid vector suitable for transformation of a plant cell and including [a] the polynucleotide according to claim 1.

33. (Twice Amended) A host cell containing a heterologous polynucleotide or nucleic acid vector comprising the isolated polynucleotide according to claim 1.

36. (Amended) A plant cell according to claim 35 having heterologous said polynucleotide [within its chromosome] in its genome.

37. (Amended) A plant cell according to claim 36 having more than one said polynucleotide per haploid genome.

38. (Twice Amended) A plant cell according to claim 35 which is comprised in a plant, a plant part or a plant propagule, or an extract [or derivative] of a plant.

39. (Amended) A method of producing [a] the host cell according to claim 33, the method including

incorporating said polynucleotide or nucleic acid vector into the cell by means of transformation.

40. (Amended) [A] The method according to claim 39 which includes recombining the polynucleotide with the cell genome nucleic acid such that it is stably incorporated therein.

41. (Twice Amended) [A] The method according to claim 39 which further includes regenerating a plant from one or more transformed cells.

42. (Twice Amended) A plant comprising [a] the plant cell according to claim 35.

45. (Amended) A method according to claim 44 further including sexually or asexually propagating or growing off-spring or a descendant of the plant regenerated from said plant cell.

46. (Twice Amended) A method of influencing [a characteristic] the growth of a plant, the method including causing or allowing expression from a heterologous

polynucleotide comprising the isolated polynucleotide according to claim 1 within cells of the plant.